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# Supplementary

Marker name	Genomic location	Existing variation	SYMBOL	Codons	Amino acids	Protein position	SIFT Score	Polyphen Score	Consequence	N
exm15449	1:11894056	rs148630210	CLCN6	Ttt/Ctt	F/L	499	deleterious(0.05)	benign(0.001)	missense_variant	1
exm15466	1:11894592	rs150830522	CLCN6	Gtg/Atg	V/M	580	deleterious(0)	possibly_damaging(0.946)	missense_variant	1
exm22932	1:17316771	rs200924194	ATP13A2	Cag/Gag	Q/E	755	deleterious(0)	possibly_damaging(0.542)	missense_variant	1
exm106217	1:155205634	-	GBA	aAc/aGc	N/S	409	deleterious(0.02)	possibly_damaging(0.891)	missense_variant	4
									splice_region_variant	
exm144887	1:207760772	-	CR1	Acg/Gcg	T/A	1858	tolerated(0.2)	probably_damaging(0.98)	missense_variant	16 (1)
exm203983	2:74592252	rs72659383	DCTN1	cGg/cAg	R/Q	1049	tolerated(0.13)	probably_damaging(1)	missense_variant	2
exm204005	2:74593944	rs150928856	DCTN1	cCt/cGt	P/R	811	deleterious(0.02)	possibly_damaging(0.848)	missense_variant	1
exm224963	2:127821511	rs143820618	BIN1	aaC/aaA	N/K	232	deleterious(0)	probably_damaging(0.998)	missense_variant	1
									splice_region_variant	
exm257473	2:202575717	rs61757691	ALS2	atA/atG	I/M	1373	deleterious(0.04)	benign(0.18)	missense_variant	3
exm257513	2:202591249	rs200706696	ALS2	gGa/gAa	G/E	1069	deleterious(0)	possibly_damaging(0.902)	missense_variant	1
exm257579	2:202619239	rs201161419	ALS2	Gat/Aat	D/N	543	deleterious(0)	probably_damaging(1)	missense_variant	1
exm257608	2:202625992	rs200733209	ALS2	aTg/aCg	M/T	242	deleterious(0)	probably_damaging(0.972)	missense_variant	2
exm362831	3:165547569	rs28933390	BCHE	gGt/gTt	G/V	418	deleterious(0.01)	benign(0.351)	missense_variant	2
exm368506	3:183975459	rs146013597	ECE2	aCg/aTg	T/M	132	deleterious_low_confidence(0)	probably_damaging(0.989)	missense_variant	2
exm368611	3:184005719	rs35875049	ECE2	cGg/cAg	R/Q	571	tolerated(0.46)	probably_damaging(0.973)	missense_variant	1
NeuroX_dbSNP_rs149515968	3:184008878	rs149515968	ECE2	Tcc/Acc	S/T	747	tolerated(0.39)	probably_damaging(0.988)	missense_variant	5
exm379355	4:845686	rs55801437	GAK	caG/caC	Q/H	1120	deleterious(0.03)	probably_damaging(0.993)	missense_variant	1
exm379592	4:898459	rs146710139	GAK	cGg/cAg	R/Q	164	deleterious(0.02)	benign(0.13)	missense_variant	2
exm390825	4:15720540	rs34163939	BST1	Ggg/Agg	G/R	239	deleterious(0.03)	probably_damaging(1)	missense_variant	1
exm461072	5:74014629	rs28942073	HEXB	cCg/cTg	P/L	417	deleterious(0.01)	benign(0.297)	missense_variant	1
exm494786	5:149456964	rs146406037	CSF1R	aAc/aTc	N/I	255	deleterious(0.03)	possibly_damaging(0.88)	missense_variant	1
exm494835	5:149460542	rs56048668	CSF1R	gTg/gGg	V/G	32	deleterious(0)	probably_damaging(1)	missense_variant	6
exm510196	5:179252184	rs11548633	SQSTM1	Aag/Gag	K/E	238	deleterious(0.02)	possibly_damaging(0.94)	missense_variant	1
exm510247	5:179263445	rs104893941	SQSTM1	cCg/cTg	P/L	392	deleterious(0)	probably_damaging(1)	missense_variant	1
exm535799	6:32497962	-	HLA-DRB5	Aag/Gag	K/E	14	deleterious(0.02)	benign(0)	missense_variant	111 (6)
exm545524	6:41129133	rs142232675	TREM2	Gat/Aat	D/N	87	tolerated(0.43)	probably_damaging(1)	missense_variant	1
exm545551	6:41162204	rs115991880	TREML2	agC/agA	S/R	248	deleterious(0.03)	benign(0.034)	missense_variant	5
exm545584	6:41166063	rs147506354	TREML2	Gtt/Ttt	V/F	54	deleterious(0)	probably_damaging(1)	missense_variant	1
exm545598	6:41166155	-	TREML2	gAc/gGc	D/G	23	deleterious(0.03)	benign(0.044)	missense_variant	88 (9)
NeuroX_dbSNP_rs121908287	6:110036336	rs121908287	FIG4	aTt/aCt	I/T	41	deleterious(0)	probably_damaging(1)	missense_variant	1
exm609425	7:23286529	rs140122424	GNPMB	cCa/cTa	P/L	18	tolerated(0.25)	probably_damaging(1)	missense_variant	5
exm609485	7:23300345	rs35363287	GNPMB	cCg/cTg	P/L	324	tolerated(0.09)	probably_damaging(0.983)	missense_variant	2
exm609529	7:23313763	rs145920361	GNPMB	Cgt/Tgt	R/C	547	deleterious(0.04)	probably_damaging(0.986)	missense_variant	1
exm614838	7:37924776	rs202221051	NME8	aGa/aCa	R/T	390	deleterious(0.01)	probably_damaging(0.996)	missense_variant	1
exm640645	7:100016781	rs141450215	ZCWPW1	gAg/gGg	E/G	105	deleterious(0)	probably_damaging(1)	missense_variant	4
exm666292	7:143088584	rs139482378	EPHA1	cGc/cAc	R/H	966	deleterious(0)	probably_damaging(1)	missense_variant	2
exm666416	7:143095849	rs140236236	EPHA1	cCg/cTg	P/L	394	deleterious(0)	probably_damaging(0.995)	missense_variant	4
exm666428	7:143095979	rs56006153	EPHA1	Cgt/Tgt	R/C	351	deleterious(0.01)	probably_damaging(0.978)	missense_variant	1
exm691577	8:27277505	rs140538134	PTK2B	Gat/Aat	D/N	100	deleterious(0.03)	probably_damaging(0.982)	missense_variant	2
exm747347	9:34635679	rs11559048	SIGMAR1	Cgg/Tgg	R/W	208	deleterious(0)	probably_damaging(1)	missense_variant	1
exm790906	9:135140063	rs202121071	SETX	Cat/Tat	H/Y	2533	deleterious(0.01)	benign(0.034)	missense_variant	1
NeuroX_9:135201718	9:135201718	-	SETX	tTt/tCt	F/S	1756	deleterious(0)	probably_damaging(1)	missense_variant	1
NeuroX_dbSNP_rs112089123	9:135202325	rs112089123	SETX	Tgt/Ggt	C/G	1554	deleterious(0.01)	benign(0.108)	missense_variant	3
exm791119	9:135204506	rs150532677	SETX	Aaa/Gaa	K/E	827	deleterious_low_confidence(0.05)	benign(0.024)	missense_variant	1
exm791198	9:135211691	rs138538492	SETX	tAt/tGt	Y/C	237	deleterious(0)	probably_damaging(1)	missense_variant	1
exm791202	9:135211747	rs117861188	SETX	aaG/aaC	K/N	218	deleterious(0.01)	probably_damaging(0.983)	missense_variant	2

exm791207	9:135218103	rs145438764	SETX	Ttg/Gtg	L/V	158	deleterious(0.01)	probably_damaging(0.999)	missense_variant	4
NeuroX_10:13174107	10:13174107	rs377219791	OPTN	gCg/gTg	A/V	481	-	probably_damaging(0.998)	missense_variant	1
NeuroX_dbSNP_rs148519599	10:73588831	rs148519599	PSAP	Cgt/Tgt	R/C	127	deleterious(0.05)	probably_damaging(0.991)	missense_variant	1
exm886203	11:6636698	rs146798796	TPP1	aAt/aTt	N/I	414	deleterious(0)	probably_damaging(0.99)	missense_variant	4
exm886228	11:6637982	rs200138397	TPP1	Cgg/Tgg	R/W	266	deleterious(0.02)	benign(0.003)	missense_variant	1
exm914223	11:59940535	rs139777263	MS4A6A	cTg/cAg	L/Q	234	deleterious(0)	probably_damaging(1)	missense_variant	1
exm914293	11:60073664	rs62000397	MS4A4A	aCc/aTc	T/I	213	deleterious(0.01)	benign(0.19)	missense_variant	1
exm964272	11:121384931	rs150609294	SORL1	aAt/aCt	N/T	371	deleterious(0)	possibly_damaging(0.507)	missense_variant	1
exm964491	11:121485586	rs117725215	SORL1	aAt/aGt	N/S	1809	tolerated(0.11)	probably_damaging(0.98)	missense_variant	1
exm964528	11:121495816	rs140327834	SORL1	gAt/gTt	D/V	2065	deleterious(0)	probably_damaging(1)	missense_variant	1
exm1034555	12:109293187	rs143550642	DAO	cGg/cAg	R/Q	283	deleterious(0)	probably_damaging(1)	missense_variant	1
exm1046873	12:123335398	rs151322438	HIP1R	gCg/gTg	A/V	152	deleterious(0.01)	possibly_damaging(0.954)	missense_variant	1
exm1046883	12:123338616	rs144603149	HIP1R	Gcc/Acc	A/T	202	tolerated(0.1)	probably_damaging(0.987)	missense_variant	1
exm1046913	12:123340138	rs149504879	HIP1R	aAt/aGt	N/S	345	deleterious(0.03)	benign(0.151)	missense_variant	1
exm1046961	12:123341637	rs140743610	HIP1R	Cgg/Tgg	R/W	564	deleterious(0.01)	probably_damaging(0.994)	missense_variant	2
exm1046974	12:123342688	rs79610396	HIP1R	Gag/Aag	E/K	619	deleterious(0.04)	possibly_damaging(0.791)	missense_variant	1
exm1072875	13:77574606	rs138611001	CLN5	aaC/aaA	N/K	242	tolerated(0.05)	probably_damaging(1)	missense_variant	17
exm1114740	14:74959940	rs147602717	NPC2	cTc/cCc	L/P	13	deleterious(0.01)	probably_damaging(0.984)	missense_variant	1
exm1122198	14:92792313	rs150573991	SLC24A4	Aca/Gca	T/A	78	deleterious(0.02)	benign(0.451)	missense_variant	1
exm1122447	14:93119307	rs143827583	RIN3	aCg/aTg	T/M	638	deleterious(0.02)	probably_damaging(1)	missense_variant	1
exm1122469	14:93142861	rs147042536	RIN3	Tat/Cat	Y/H	793	deleterious(0)	probably_damaging(1)	missense_variant	6
exm1157672	15:44918698	rs144012151	SPG11	aTt/aCt	I/T	692	deleterious(0)	possibly_damaging(0.89)	missense_variant	1
exm1157728	15:44949354	rs80338868	SPG11	Gtt/Att	V/I	270	tolerated(0.13)	probably_damaging(0.975)	missense_variant	8
NeuroX_dbSNP_rs148199798	15:72641570	rs148199798	HEXA	tCt/tGt	S/C	279	deleterious(0.01)	probably_damaging(0.991)	missense_variant	1
exm1174638	15:72642925	rs121907970	HEXA	Cgg/Tgg	R/W	247	deleterious(0)	probably_damaging(1)	missense_variant	1
exm1229460	16:28488944	rs146610181	CLN3	Cac/Aac	H/N	404	deleterious(0.02)	probably_damaging(0.999)	missense_variant	2
exm1229500	16:28498845	rs144770450	CLN3	aGt/aAt	S/N	131	deleterious(0)	probably_damaging(0.958)	missense_variant	1
exm1282264	17:4849268	rs140547520	PFN1	gAa/gGa	E/G	117	deleterious(0)	probably_damaging(1)	missense_variant	2
exm1313053	17:34149718	-	TAF15	tAt/tGt	Y/C	122	deleterious_low_confidence(0)	possibly_damaging(0.943)	missense_variant	2
exm1313094	17:34171358	-	TAF15	cGt/cAt	R/H	388	deleterious_low_confidence(0)	probably_damaging(0.999)	missense_variant	2
exm1344029	17:61557724	rs141543325	ACE	Cgc/Tgc	R/C	228	deleterious(0)	probably_damaging(1)	missense_variant	1
exm1344069	17:61559850	rs150466411	ACE	aCg/aTg	T/M	381	deleterious(0)	probably_damaging(1)	missense_variant	1
exm1344071	17:61559883	rs138418851	ACE	aTg/aCg	M/T	392	deleterious(0)	probably_damaging(0.999)	missense_variant	1
exm1344136	17:61562654	rs147429960	ACE	tCc/tGc	S/C	660	deleterious(0.01)	probably_damaging(0.984)	missense_variant	3
exm1344195	17:61568577	rs3730043	ACE	aCg/aTg	T/M	916	deleterious(0)	probably_damaging(1)	missense_variant	10
exm1344206	17:61570816	rs141750591	ACE	Gtg/Atg	V/M	978	deleterious(0)	probably_damaging(1)	missense_variant	1
exm1378433	18:21118528	rs80358257	NPC1	Cct/Gct	P/A	1007	deleterious(0)	probably_damaging(1)	missense_variant	1
exm1378449	18:21119839	rs34302553	NPC1	Ggc/Agc	G/S	911	tolerated(0.14)	probably_damaging(0.999)	missense_variant	2
exm1381184	18:29104714	-	DSG2	Ata/Gta	I/V	293	deleterious(0)	possibly_damaging(0.932)	missense_variant	62 (5)
exm1381259	18:29126108	rs142841727	DSG2	gTa/gGa	V/G	920	tolerated(0.51)	probably_damaging(0.967)	missense_variant	10
exm1398807	19:1043793	rs146086314	ABCA7	Cgg/Tgg	R/W	334	deleterious(0)	probably_damaging(0.976)	missense_variant	1
exm1398864	19:1047169	rs144852598	ABCA7	cTc/cCc	L/P	620	deleterious(0)	probably_damaging(1)	missense_variant	2
exm1398911	19:1049360	rs199517653	ABCA7	Ggg/Agg	G/R	826	tolerated(0.15)	probably_damaging(0.992)	missense_variant	1
exm1398927	19:1051006	rs143718918	ABCA7	cGg/cAg	R/Q	880	deleterious(0)	probably_damaging(1)	missense_variant	3
NeuroX_dbSNP_rs145632609	19:1056941	rs145632609	ABCA7	tGt/tAt	C/Y	1541	deleterious(0)	probably_damaging(1)	missense_variant	2
exm1399104	19:1057343	rs117187003	ABCA7	Gtg/Atg	V/M	1599	deleterious(0.02)	probably_damaging(1)	missense_variant	5
exm1399110	19:1057960	rs141237099	ABCA7	Gtg/Atg	V/M	1643	deleterious(0.02)	probably_damaging(0.965)	missense_variant	1
exm1399140	19:1059056	rs114782266	ABCA7	cGc/cAc	R/H	1812	deleterious(0.04)	benign(0.049)	missense_variant	13
exm1436897	19:15289850	rs55882518	NOTCH3	cAt/cTt	H/L	1235	deleterious(0.02)	benign(0)	missense_variant	7
exm1436908	19:15290007	rs10408676	NOTCH3	Gtg/Atg	V/M	1183	deleterious(0.02)	possibly_damaging(0.747)	missense_variant	3
exm1436916	19:15290236	-	NOTCH3	caC/caA	H/Q	1133	deleterious(0)	possibly_damaging(0.66)	missense_variant	18
exm1437060	19:15302941	rs147373451	NOTCH3	cAt/cGt	H/R	170	deleterious(0.01)	possibly_damaging(0.776)	missense_variant	4
exm1523061	20:3869884	rs148036492	PANK2	gAt/gTt	D/V	46	deleterious_low_confidence(0.03)	benign(0)	missense_variant	2
NeuroX_rs41279408	20:3903937	rs41279408	PANK2	cCg/cTg	P/L	570	deleterious_low_confidence(0)	probably_damaging(0.981)	missense_variant	1
exm1551807	20:55033660	rs150016338	CASS4	Ctc/Ttc	L/F	740	tolerated(0.49)	probably_damaging(0.993)	missense_variant	0 (1)

exm1552869	20:57016076	rs143144050	VAPB	atG/atA	M/I	170	deleterious(0.04)	benign(0.154)	missense_variant	2
NeuroX_dbSNP_rs139312819	20:62560745	rs139312819	DNAJC5	gCg/gTg	A/V	63	deleterious(0)	probably_damaging(1)	missense_variant	1
NeuroX_21:33038771	21:33038771	-	SOD1	aGt/aTt	S/I	60	deleterious(0)	probably_damaging(0.999)	missense_variant	1
exm2007036	22:32894494	rs34316445	FBXO7	Gat/Cat	D/H	516	deleterious(0)	possibly_damaging(0.894)	missense_variant	2
exm2010252	22:38522424	rs76718524	PLA2G6	Cgg/Tgg	R/W	461	deleterious(0.04)	probably_damaging(0.999)	missense_variant	1
exm1608187	22:38541545	rs142530390	PLA2G6	Cac/Gac	H/D	109	deleterious(0.01)	benign(0.037)	missense_variant	0 (1)
exm1649673	X:100653420	-	GLA	Gat/Tat	D/Y	313	deleterious(0)	probably_damaging(0.999)	missense_variant	4

## Supplementary Table 1

### Predicted pathogenic variants identified

108 variants predicted to be pathogenic in neurologic and neurodegenerative genes. Those highlighted in grey are located in genes that have previously been associated with Alzheimer's disease using GWAS. The name of the probe on the NeuroX (Marker name) is followed by variant information genotyped by this probe, including the genomic position (Genomic location) of the variant (in genome build GRCh37), the reference single nucleotide polymorphism identifier (Ref SNP), and the gene it resides in (Gene). The variant is given at nucleotide level (Base Change) on the sense strand and amino acid level (Protein Change) which is written using the conventional 1-letter amino acid code. The variant effect and confidence score are given from SIFT and Polyphen along with the consequence(s) at the transcript level (Consequence). Finally the number of heterozygote in sEOAD samples is given in the final column (N) with the number of homozygous mutant samples given in brackets where applicable.

Marker name	Base Position
NeuroX_GRN_Ala237fs	4031641
NeuroX_GRN_Asn118fs	42427596
NeuroX_GRN_Asn119del	42427601
NeuroX_GRN_Thr52Hisfs	42426809
NeuroX_LRRK2_Glu2490fs	40761451
NeuroX_LRRK2_IVS30-6C_T	40704227
NeuroX_LRRK2_IVS31+3A_G	40704454
NeuroX_LRRK2_IVS32+14G_A	40707989
NeuroX_LRRK2_IVS33+6T_A	40709108
NeuroX_LRRK2_IVS37-9A_G	40716953
NeuroX_LRRK2_IVS38+7C_T	40717115
NeuroX_LRRK2_IVS46-14T_A	40753048
NeuroX_LRRK2_IVS46-8delT	40753054
NeuroX_PARK2_Ala291fs	161990449
NeuroX_PARK2_Asn428fs	161781121
NeuroX_PARK2_Cys238fs	162394356
NeuroX_PARK2_Cys323fs	161969996
NeuroX_PARK2_Gln34fs_del_A	162864412
NeuroX_PARK2_Gln34fs_del_AG	162864411
NeuroX_PARK2_Gly179fs	162475205
NeuroX_PARK2_Pro133del	162683570
NeuroX_PARK2_Trp74fs	162683748
NeuroX_PARK2_Val324fs	161969998
NeuroX_PARK7_Pro158del	8045015
NeuroX_PINK1_23bp_del_ex7	20975486
NeuroX_PINK1_534_535insQ	20977040
NeuroX_PINK1_Asp525fs	20977011
NeuroX_PINK1_Cys549fs	20977085
NeuroX_PINK1_Lys520fs	20976995

## Supplementary Table 2

### Markers with updated base position

List of 29 markers which had their genomic base position updated from zero to their correct base position (genome build GRCh37)

Marker name
exml624485
exml624661
exml624677
exml624783
exml624797
exml624862
exml624867
exml624886
exml624907
exml624944
exml624960
exml624975
exml624995
exml624999_ver3
exml625001
exml625200
exml625277
exml625538
exml625569
exml625571
exml625573
exml648538
exml667350
exml667504
exml667508
exml667537
exml667541
exm2262791
exm2263170
exm2263174
exm2263176
exm2263276
exm2263278_ver3
exm2263279
exm2263280
exm2263281
exm2268448
exm2273075
exm2273161
exm2273221
exm2273222
exm2273223
exm2273224
exm2273278
exml624939_ver2
exml624946
exml625030_ver4
exm-rs5941436_ver2
exm-rs2573905
exml625510
exm2264787
exm-rs525869_ver4
exml624877
exml667344
exm2273163
exm2273277
exm2264764
exml624934
exml667357
exml625534
exml625323
exml624879
exml624887
exml648651
exml625041
exml625556_ver2
exml624641
exml625029
exml625819

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exml624434  
exml625064  
exml625554  
exml625555\_ver3  
exml625807  
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exml667360  
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exml624766  
exml625068  
exml625216  
exml625222  
exml625253  
exml648569  
exm2208735  
exml624792  
exml624794  
exml624804  
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exml625025\_ver2  
exml625046  
exml625162  
exml625204  
exml625383\_ver2  
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exml624953  
exml624965  
exml624996\_ver3  
exml625022  
exml625063  
exml625610  
exml625631  
exml648554  
exml667351  
exml667363  
exm2209863  
exm2248602  
exm2248962

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### **Supplementary Table 3**

#### **Markers with updated chromosome**

List of 121 markers updated to the pseudoautosomal region (XY)

						Pathogenic Nature Unclear			Causative			Not Pathogenic		
Database	Gene	Disease	Database	Designed on NeuroX	Passed QC	Database	Designed on NeuroX	Passed QC	Database	Designed on NeuroX	Passed QC	Database	Designed on NeuroX	Passed QC
ADFTDPD	APP	AD	31	10	10	6	3	3	24	6	6	1	1	1
	C9orf72	ALS/FTD	12	0	0	11	0	0	0	0	0	1	0	0
	CHMP2B	FTD	12	7	7	4	0	0	4	3	3	4	4	4
	FUS	ALS	44	21	20	18	3	3	22	15	15	4	3	2
	GRN	FTD	146	33	33	45	10	10	66	13	13	35	10	10
	LRRK2	PD	128	71	71	54	15	15	6	3	3	68	53	53
	MAPT	FTD	73	11	10	27	10	9	44	1	1	2	0	0
	PARK2	PD	144	70	70	22	4	4	59	27	27	63	39	39
	PARK7	PD	21	6	5	5	1	0	1	0	0	15	5	5
	PINK1	PD	130	52	52	30	12	12	20	7	7	80	33	33
	PSEN1	AD	197	76	74	4	3	3	185	69	67	8	4	4
	PSEN2	AD	25	9	9	5	1	1	13	5	5	7	3	3
	SNCA	PD	5	1	1	1	1	1	3	0	0	1	0	0
HPP	TARDBP	ALS	45	26	26	9	3	3	34	21	21	2	2	2
	VCP	FTD	20	14	14	0	0	0	18	13	13	2	1	1
	PRNP	Prion	42	5	5	18	4	4	24	1	1	0	0	0
Total	16		1075	412	407	259	70	68	523	184	182	293	158	157

#### Supplementary Table 4

##### Coverage on the NeuroX of variants from familial online databases

Pathogenic nature and NeuroX coverage of all variants from online databases; these include the AD&FTD mutation database and PD mutation database (ADFTDPD), and the Human Prion Protein Database (HPP). All variants from the online databases are clustered into the gene they reside in (Gene) and the disease most associated (Disease). The number of variants in each gene is given (Database), followed by the number designed on the NeuroX (Designed on NeuroX) and finally the number that passed quality control in our dataset (passed QC). These variants are then subcategorised depending on the pathogenicity; those that have unclear pathogenic nature (Pathogenic Nature Unclear), those that cause disease (Causative), and those that do not cause disease (Not Pathogenic). Key: AD; Alzheimer's disease, FTD; frontotemporal dementia, ALS; amyotrophic lateral sclerosis, PD; Parkinson's disease.